

2011 Military Health System Conference

Innovations in Wound Infection Prevention and Management and Antimicrobial Countermeasures

The Quadruple Aim: Working Together, Achieving Success

COL Duane Hospenthal, Infectious Disease Consultant to the Army Surgeon General

24 January 2011



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Wound Infection Prevention and Management - **The Problem**



- Complex traumatic injuries are often complicated by multidrug-resistant (MDR) bacterial infections and colonization
 - Resulting in increased morbidity and mortality
 - Increased use of broad spectrum antimicrobials and older and/or more toxic agents (e.g., colistin and aminoglycosides)

Wound Infection Prevention and Management - Definitions



- MDR bacteria – multidrug-resistant bacteria
- MDRO – multidrug-resistant organisms
 - Typically, gram negative rods
 - *Acinetobacter*, *E. coli*, *Enterobacter*, *Klebsiella*, *Pseudomonas*
 - Also, gram positive cocci
 - Methicillin-resistant *Staphylococcus aureus* (MRSA)
 - Vancomycin-resistant *Enterococcus* (VRE)

Wound Infection Prevention and Management - **Solutions**



- Prevention
 - Prevention of infection
 - Prevention of colonization
- Management
 - New diagnostic modalities
 - New treatment modalities

Wound Infection Prevention and Management - **Solutions**



- Prevention
 - Prevention of infection
 - Prevention of colonization
 - Epidemiology
 - Pathophysiology
- Management
 - New diagnostic modalities
 - New treatment modalities

Wound Infection Prevention and Management - **Solutions**



- Prevention
 - Prevention of infection
 - Prevention of colonization
 - Epidemiology
 - Pathophysiology
- Management
 - New diagnostic modalities
 - New treatment modalities
 - Epidemiology
 - Pathophysiology

Wound Infection Prevention and Management - Outline



- Current epidemiology
- Prevention efforts
- Management efforts

Wound Infection Prevention and Management

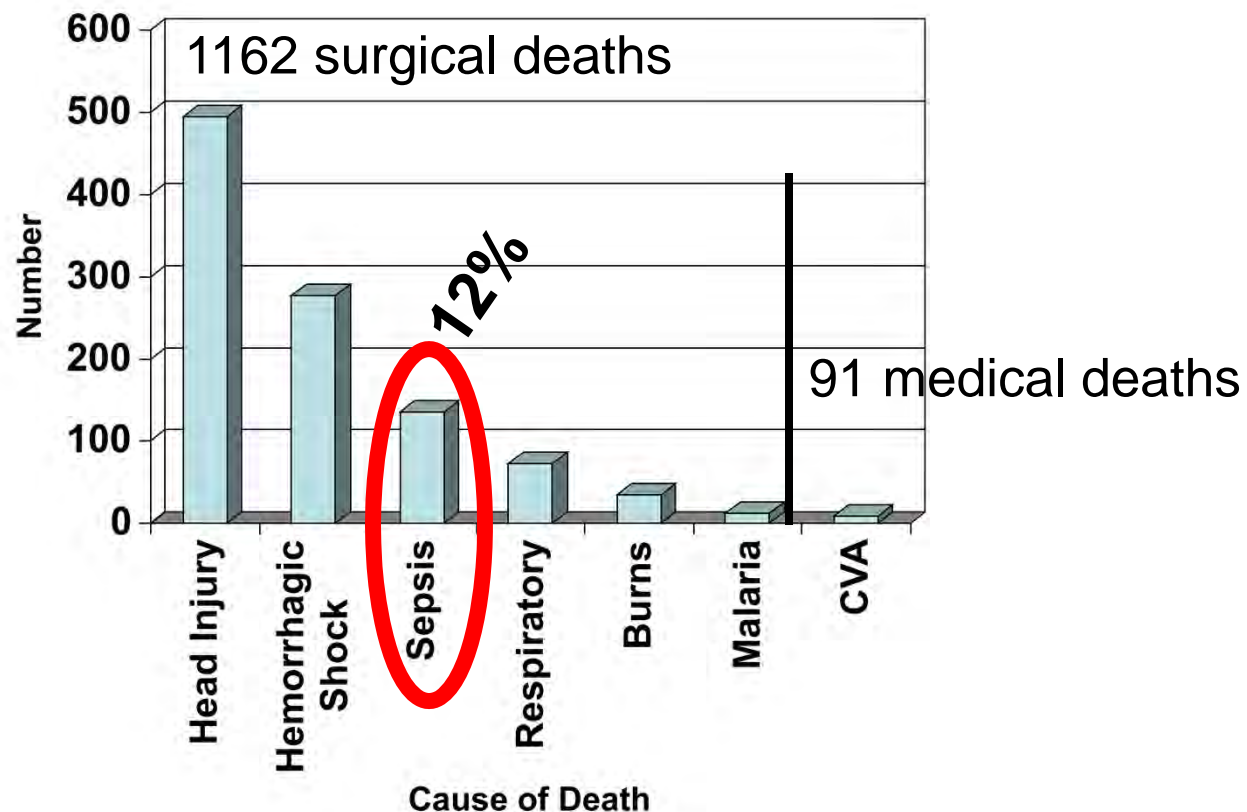


- Current epidemiology
- Prevention efforts
- Management efforts

Wound Infection Prevention and Management - Epidemiology



Combat Hospital - Vietnam



Arnold. Mil Med 1978;143:161

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of 132,996 admissions

Wound Infection Prevention and Management - Epidemiology



- Association of infection with trauma (Joint Theater Trauma Registry, JTTR)

	Odds ratio	95% CI
Bomb	9.78	1.81-54.82
Landmine	4.00	1.29-2.4
ISS score > 29	3.76	2.47-5.73
ISS score 15-29	2.33	1.56-3.50
Explosive device	1.86	1.04-3.33

Murray. J Trauma 2009;66:S138

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Wound Infection Prevention and Management - Epidemiology



- Infections associated with combat-injury
- Trauma Infectious Disease Outcome Study (TIDOS) (NIAID-USU IDCRP)

	ICU	Ward	Total
Patients	64	128	192
Infections	28 (43.8%)	19 (14.8%)	47 (24.5%)
Bloodstream	12 (18.8%)	6 (3.9%)	17 (8.9%)
Skin/soft tissue	16 (23.4%)	12 (9.4%)	27 (14.1%)
Osteomyelitis	8 (12.6%)	6 (4.7%)	14 (7.3%)

Wound Infection Prevention and Management - **Epidemiology**



- Acinetobacter and other MDR pathogens
 - Hospital-acquired infections in Turkey
 - Ventilator-associated pneumonias in Lebanon
 - Nosocomial bacteremia in Israel
 - ICU infections in Kuwait



Wound Infection Prevention and Management - **Epidemiology**



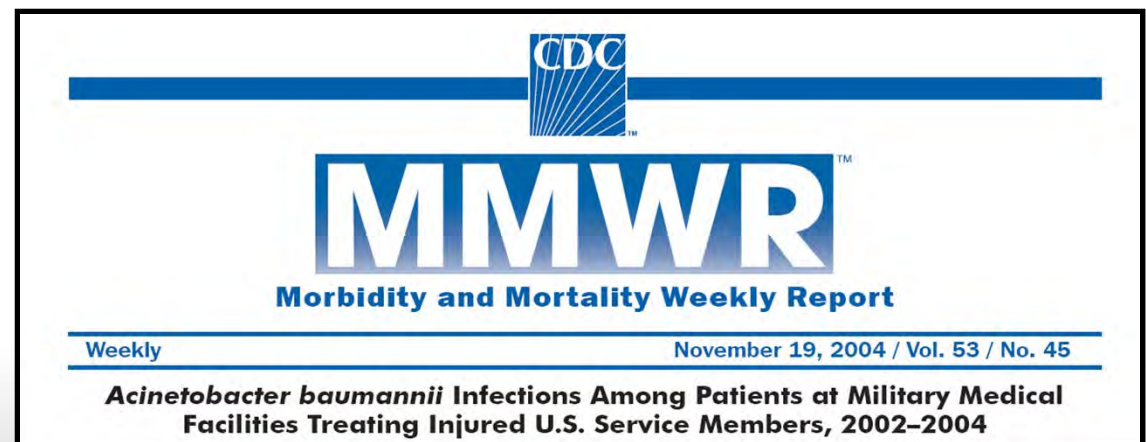
- USNS Comfort, March-May 2003
- 211 trauma patients (85% Iraqi) - 56 infected
 - Injury to admission - avg. 4.2 days
 - *Acinetobacter* - 33%



Petersen. Ann Surg 2007;245:803

CDC. MMWR 2004;53:1063

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Wound Infection Prevention and Management - **Epidemiology**



- Virulence of MDR *Acinetobacter* (USAISR burn patients). Mortality with bacteremia

Organism	OR	95% CI	p
<i>P. aeruginosa</i>	2.25	0.96 - 5.30	0.061
<i>K. pneumoniae</i>	2.71	1.14 - 6.49	0.025
<i>Acinetobacter</i>	0.48	0.21 - 1.11	0.084
<i>S. aureus</i>	0.79	0.30 - 2.06	0.628
any MDR	2.78	1.13 - 6.83	0.026

Ressner. J Am Coll Surg 2006;203:439

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Wound Infection Prevention and Management - **Epidemiology**



- *Acinetobacter* virulence (extremity trauma)

Organisms	Initial	Relapse
<i>Acinetobacter</i>	13	0
<i>Enterobacter</i>	6	0
<i>Pseudomonas</i>	5	3
<i>E. coli</i>	2	1
CoN <i>Staphylococcus</i>	3	7
<i>Staphylococcus aureus</i>	3	9
<i>Enterococcus</i>	3	0

Johnson. Clin Infect Dis 2007;45:409

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Wound Infection Prevention and Management - **Epidemiology**



- Fungal pathogens causing invasive infections
- WRAMC - 2002-2008
- 0.4 cases/1,000 admissions (n=6)
- Moulds - *Aspergillus* (4), *Bipolaris* (2), *Mucor* (1), *Absidia* (1)

Wound Infection Prevention and Management - **Epidemiology**



- Where are all the Acinetobacter and other MDR bacteria coming from?

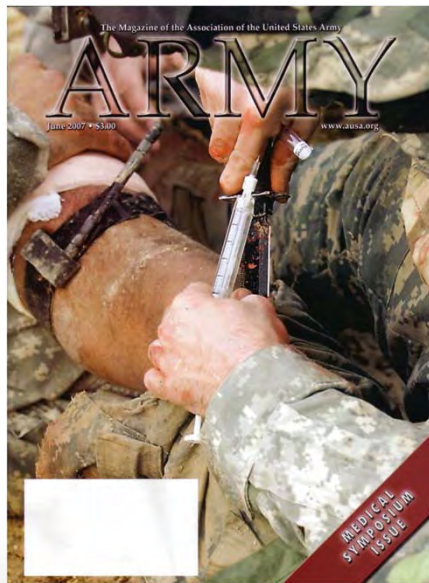
Wound Infection Prevention and Management - Epidemiology



- Theories
 - Pre-injury colonization
 - Inoculation at time of injury from environment
 - Nosocomial transmission



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Wound Infection Prevention and Management - **Epidemiology**



- Pre-injury colonization
 - Fort Sam Houston, 100 Soldiers
 - *Acinetobacter* detected in 17 (17%)
 - Phenotypes/genotypes unlike clinical isolates
 - Repeat study in Iraq detected 0/107 (0%)
 - Fort Sam Houston, 812 Soldiers
 - Community-acquired MRSA detected in 24 (3%)
 - MDRO carried into battle

Griffith. Infect Control Hosp Epidemiol 2006;27:659

Griffith. Infect Control Hosp Epidemiol 2007;28:720

Ellis. Clin Infect Dis 2004;39:971

Wound Infection Prevention and Management - **Epidemiology**



- Environmental contamination?
 - Wound of Soldiers, Baghdad CSH, Iraq
 - 49 casualties - 61 wounds
 - 37 of 40 recovered bacteria
 - Gram positive skin flora (including 2 MRSA)
 - No gram negative MDR bacteria recovered



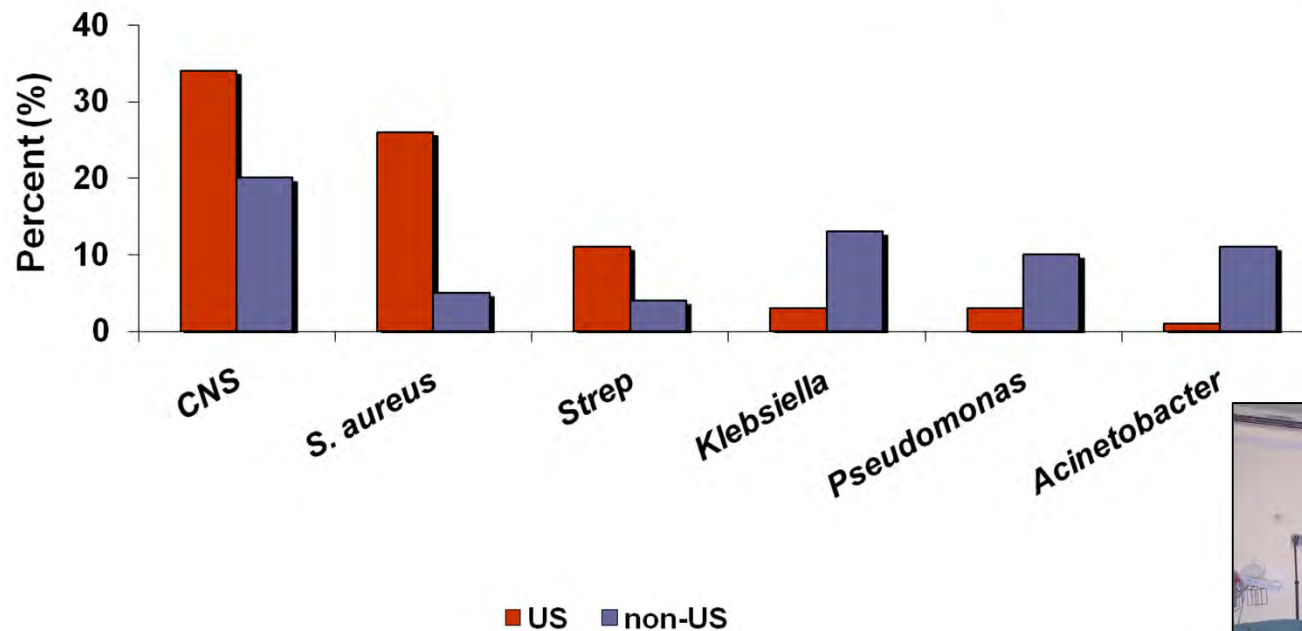
Murray. Mil Med 2006;171:826

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Wound Infection Prevention and Management - Epidemiology



- Nosocomial transmission?
 - Cultures from an deployed CSH (Iraq)



Yun. Mil Med 2006;171:821

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Wound Infection Prevention and Management - **Epidemiology**



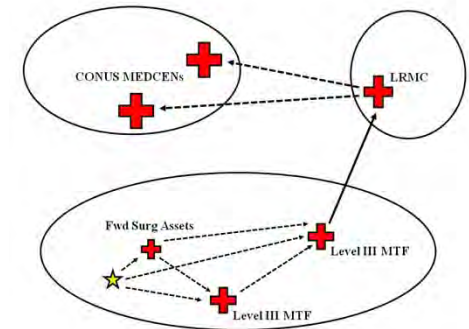
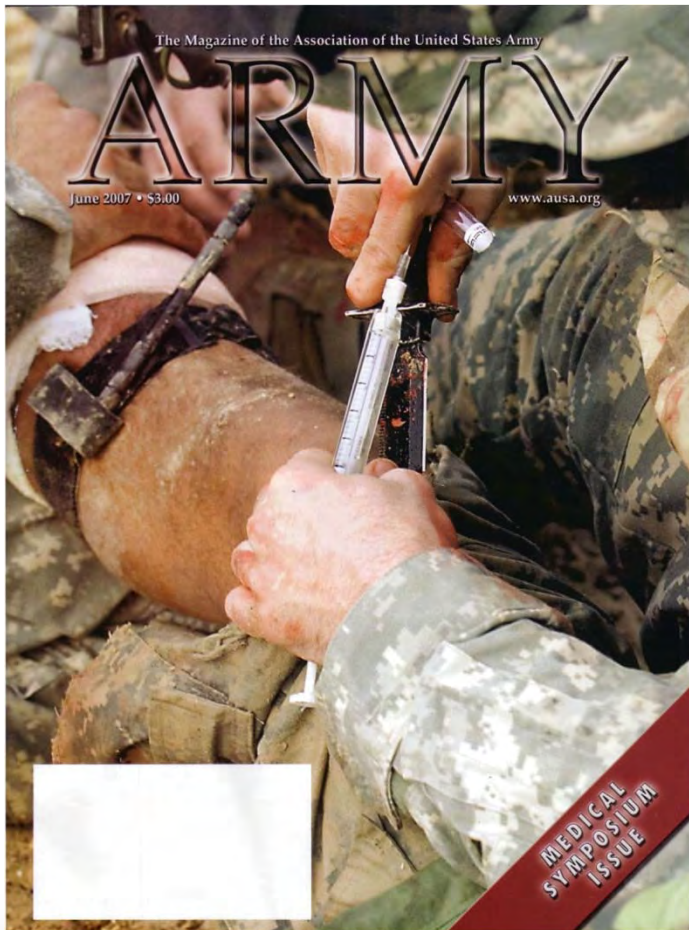
- MDR bacteria recovered from local nationals in both Iraq and Afghanistan at admission
 - Large number of MDR *E. coli* in Afghanistan

Ake. IDSA 2009

Sutter. IDSA 2009

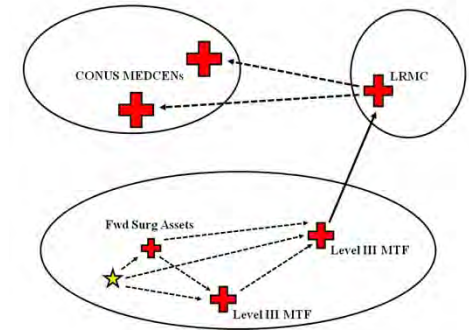
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Wound Infection Prevention and Management - Epidemiology

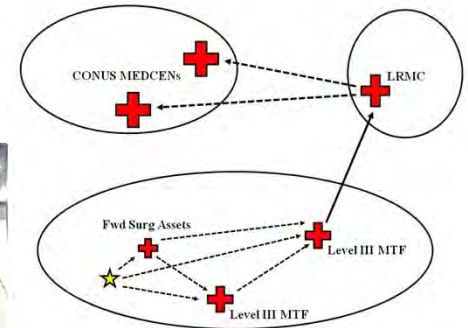
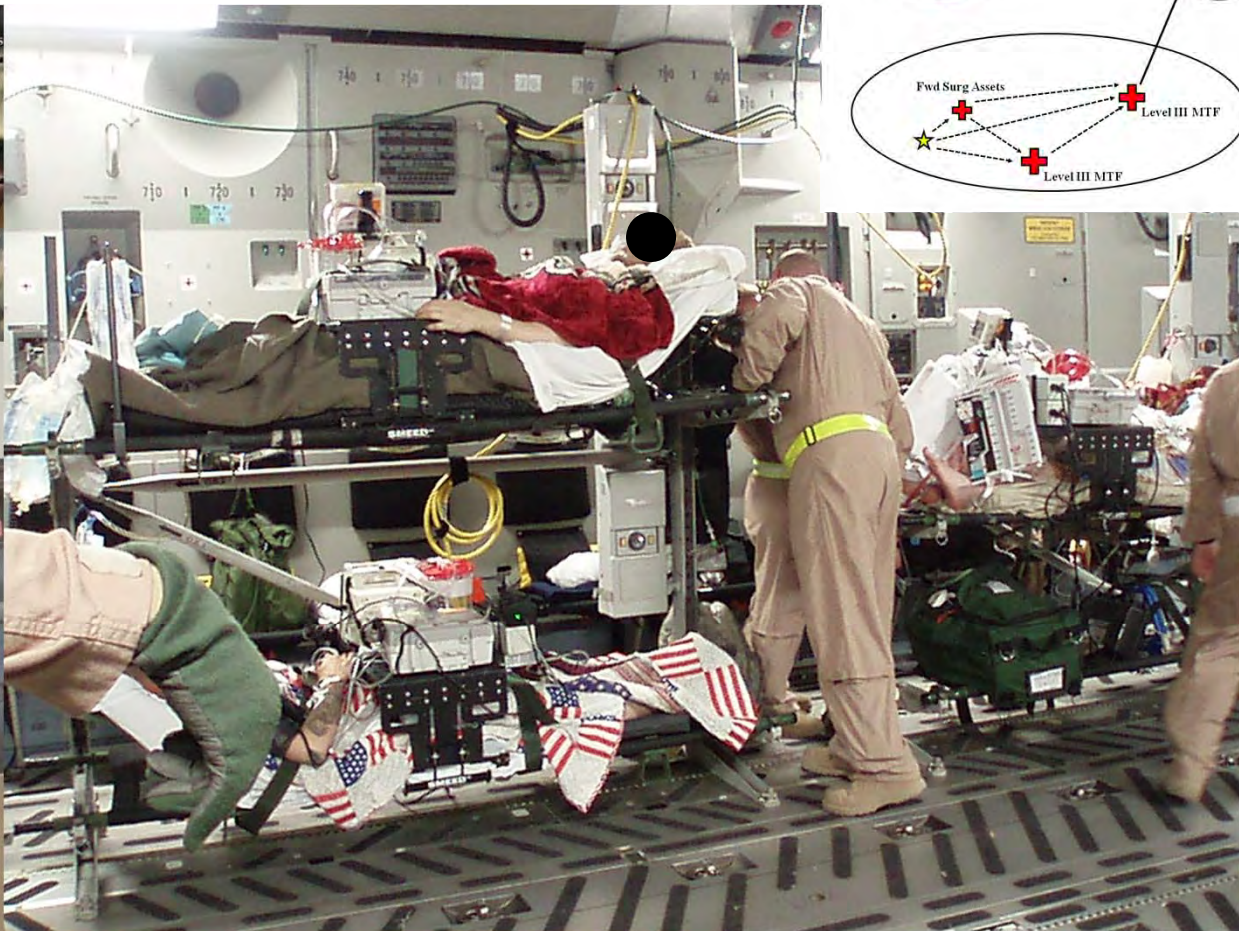


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Wound Infection Prevention and Management - Epidemiology



Wound Infection Prevention and Management - Epidemiology

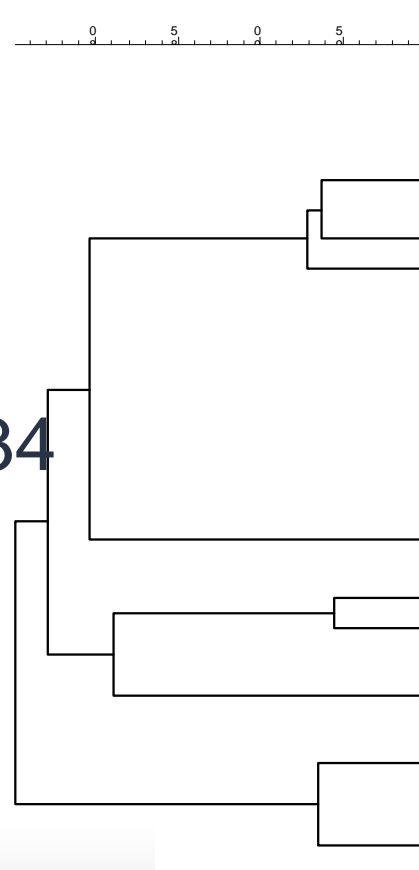


Wound Infection Prevention and Management - Epidemiology



- PFGE strains
 - 66 different strains among 170 clinical isolates
 - 25 different strains among 34 environmental isolates

Done (Opt:5.00%) (Tol 1.5%-1.5%) (H>0.0% S>0.0%) [0.0%-100.0%]
PFGE_III



PFGE_III

OIFC332	Dogwood	B
OIFC022	WRAMC	B
OIFC037	WRAMC	B
OIFC063	WRAMC	B
OIFC109	WRAMC	B
OIFC188	WRAMC	B
OIFC054	WRAMC	B
OIFC094	WRAMC	B
OIFC033	WRAMC	A
OIFC052	LRMC	A
OIFC034	Comfort	A
OIFC086	WRAMC	A
OIFC088	Comfort	A
OIFC100	Baghdad	A
OIFC103	LRMC	A
OIFC141	WRAMC	A
OIFC165	Comfort	A
OIFC167	Comfort	A
OIFC303	Kuwait	E
OIFC162	LRMC	E
OIFC316	Mosul	D
OIFC330	Dogwood	D
OIFC131	LRMC	D
OIFC099	Baghdad	C
OIFC124	WRAMC	C
OIFC028	LRMC	C
OIFC032	LRMC	C
OIFC147	WRAMC	C

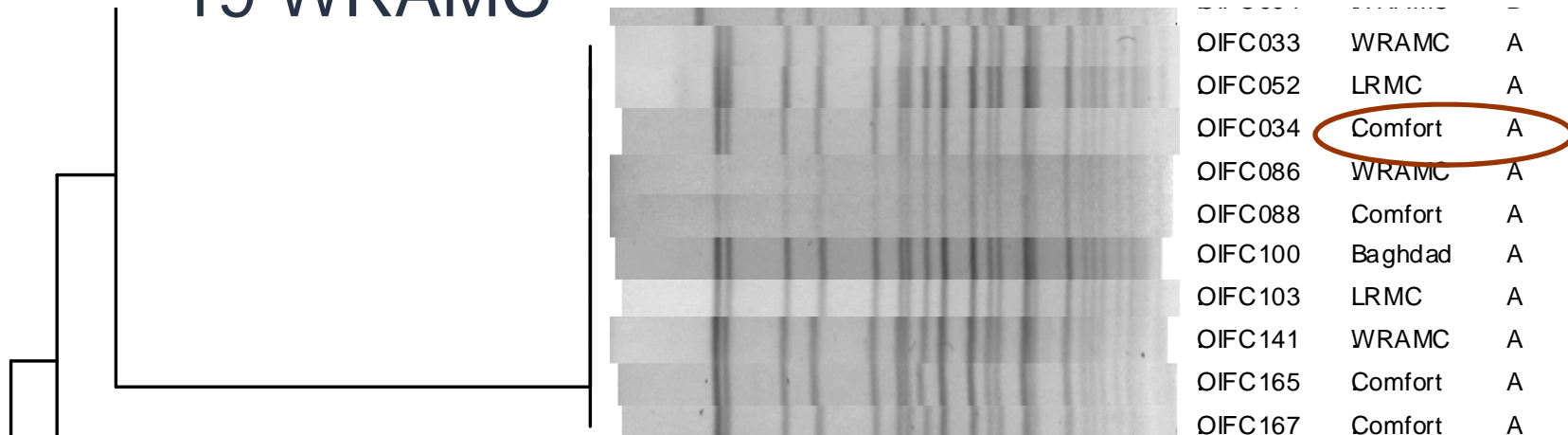
Scott. Clin Infect Dis 2007;44:1577

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Wound Infection Prevention and Management - Epidemiology



- A strain
 - Environmental sample from a CSH Operating room
 - 43 patients- 2 Baghdad, 18 Comfort, 6 LRMC, 19 WRAMC



Scott. Clin Infect Dis 2007;44:1577

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Wound Infection Prevention and Management - **Epidemiology**

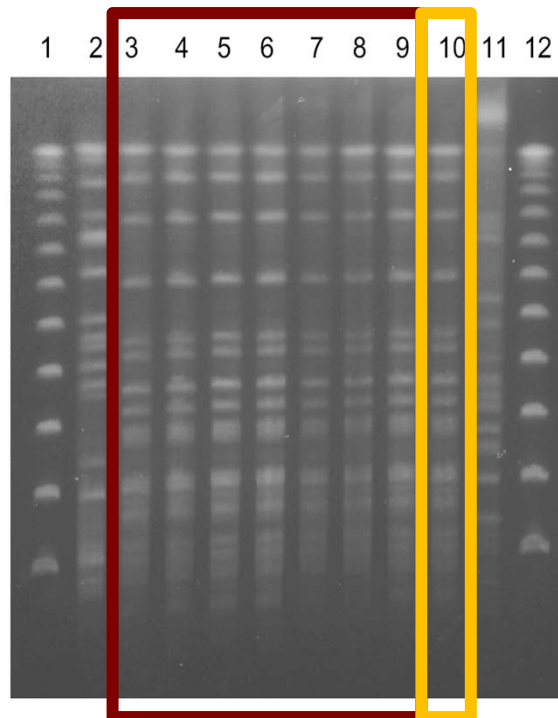


- *Acinetobacter* recovered from Canadian soldiers treated in Afghanistan after return to Canada



Tien . BMC Infect Dis 2007;7:95

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Lane 10 - ventilator air filter (Kandahar)

Wound Infection Prevention and Management - Epidemiology



54 Screened in **Iraq** - 1 MRSA

→ 0%



50 Screened in **Germany** (2.8 days) - 1 *Acinetobacter*

→ 2%



32 Screened in the **US** (7.9 days) - 1 ESBL-producing *Klebsiella pneumoniae*, 2 MRSA, 3 *Acinetobacter*

→ 10%



9 Infections in the **US** (11.6 days) - 1 ESBL-producing *Klebsiella pneumoniae*, 7 *Acinetobacter*

Wound Infection Prevention and Management - **Epidemiology**



- Also, within CONUS within our MEDCENs
- 22% of patients developed new colonization with MDRO after admission to WRAMC

Weintrob. Infect Control Hosp Epidemiol 2010;31:330

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Wound Infection Prevention and Management - **Epidemiology**



- Incidence/prevalence of MDR infections?
 - No ICD-9 code for *Acinetobacter* infection
 - No ICD-9 codes for MDR Gram negative bacteria infections

Wound Infection Prevention and Management - **Epidemiology**

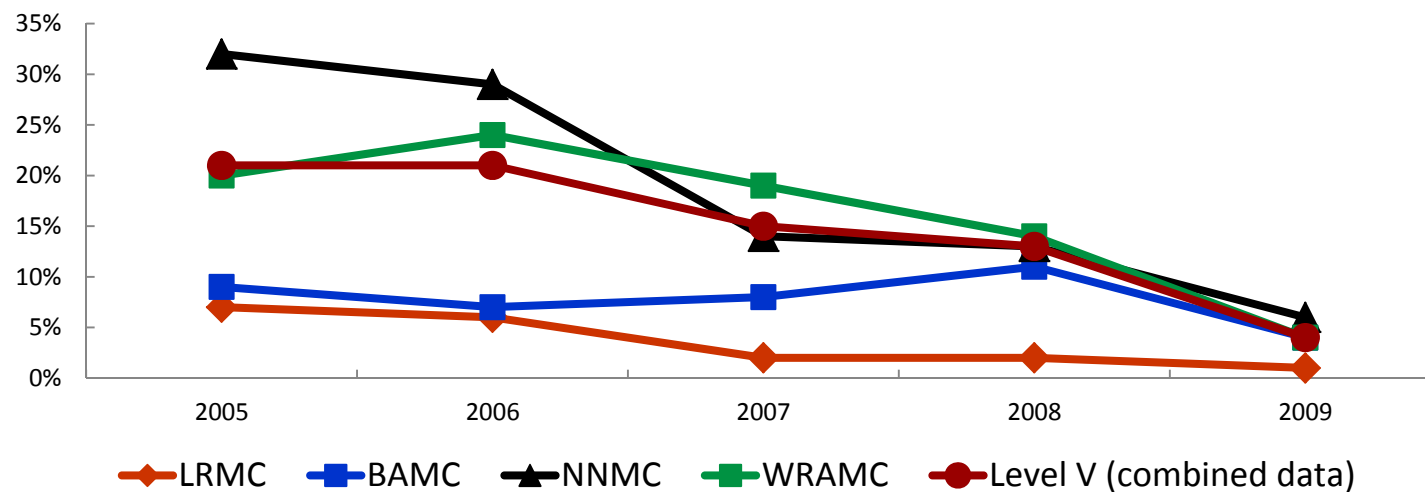


- Admission colonization screening
 - BAMC/LRMC/NNMC/WRAMC collaboration
 - Produce potentially actionable data
 - For individual patient care/local infection control
 - For feedback upstream
 - 2003-2008, screening not standardized, *Acinetobacter* only
 - Fall 2008-present, screening standardized, expanded to all MDR bacteria

Wound Infection Prevention and Management - Epidemiology



- 2005-09, 18,560 of 21,272 admits screened
- *Acinetobacter* colonization declined
 - LRMC, 7% to 1%; Level V, 21% to 4%



Wound Infection Prevention and Management - Epidemiology



■ MDR screening (2009)

	LRMC	BAMC	NNMC	WRAMC	Total
Personnel screened	2256	169	193	371	2989
Personnel MDR positive	78	27	23	43	171
Colonization rate	3%	16%	12%	12%	6%
<i>Acinetobacter</i> species	18	7	11	14	50
<i>Escherichia coli</i> (ESBL)	52	11	10	25	98
<i>Klebsiella</i> species (ESBL)	7	8	0	3	18
MRSA	1	1	2	0	4
<i>Pseudomonas aeruginosa</i>	1	0	0	0	1

Wound Infection Prevention and Management - Epidemiology



■ MDR screening (2009)

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Wound Infection Prevention and Management - **Epidemiology**



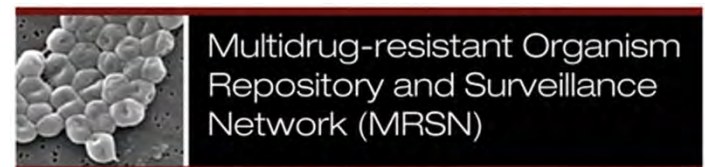
- Joint Theater Trauma Registry (JTTR)
Infectious Disease module
 - Improved clarity to define epidemiology
 - Tool for study of injury-associated infections and best care/interventions



Wound Infection Prevention and Management - **Epidemiology**



- Multidrug-resistant Organism Repository and Surveillance Network (MRSN)
 - Improved clarity to define epidemiology
 - Phenotypic and genotypic characterization of bacterial isolates
 - Resource for MTF outbreaks



WRAIR

Walter Reed Army
Institute of Research

Soldier Health • World Health

Wound Infection Prevention and Management



- Current epidemiology
- Prevention efforts
- Management efforts



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Wound Infection Prevention and Management - Prevention



- Standardization of care practices
 - Guidelines
 - Use on national/international guidelines
 - Development of combat-specific guidelines
 - Standardization of theater infection control (IC) program/procedures (SOPs)
 - Trained IC officers (ICOs) in theater
- Emphasis on IC basics in theater
- Clinical microbiology in theater

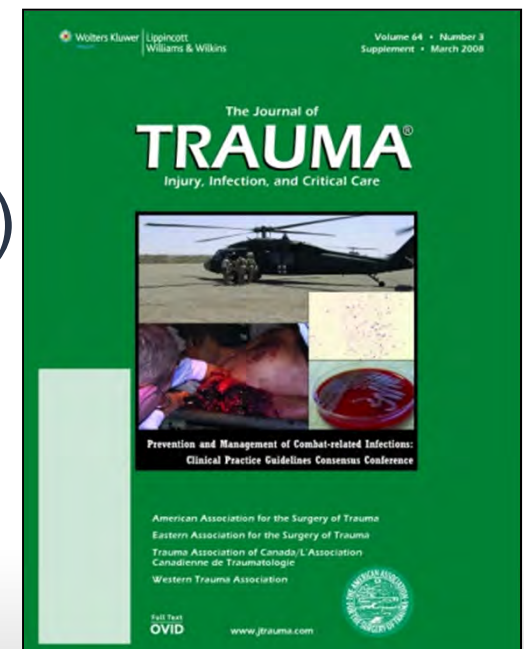
Wound Infection Prevention and Management - Prevention



- Clinical practice guidelines
 - Consensus conference (Jun07)
 - Production of clinical practice guidelines – “Guidelines for Prevention of Infection after Combat-related Injuries” (Mar08)
 - Basis for JTTS guidelines (Mar10)
 - Update consensus conference (Jan11)

Hospenthal. J Trauma 2008;64:S211

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Wound Infection Prevention and Management - Prevention



- Clinical practice guidelines
 - Rapid evacuation to surgical care (irrigation/debridement)
 - Limit antibiotic spectrum/duration around wound management
 - Emphasize basic infection control efforts to prevent spread from other hospitalized patients and to decrease antibiotic pressure selecting for resistant organisms

Wound Infection Prevention and Management - Prevention

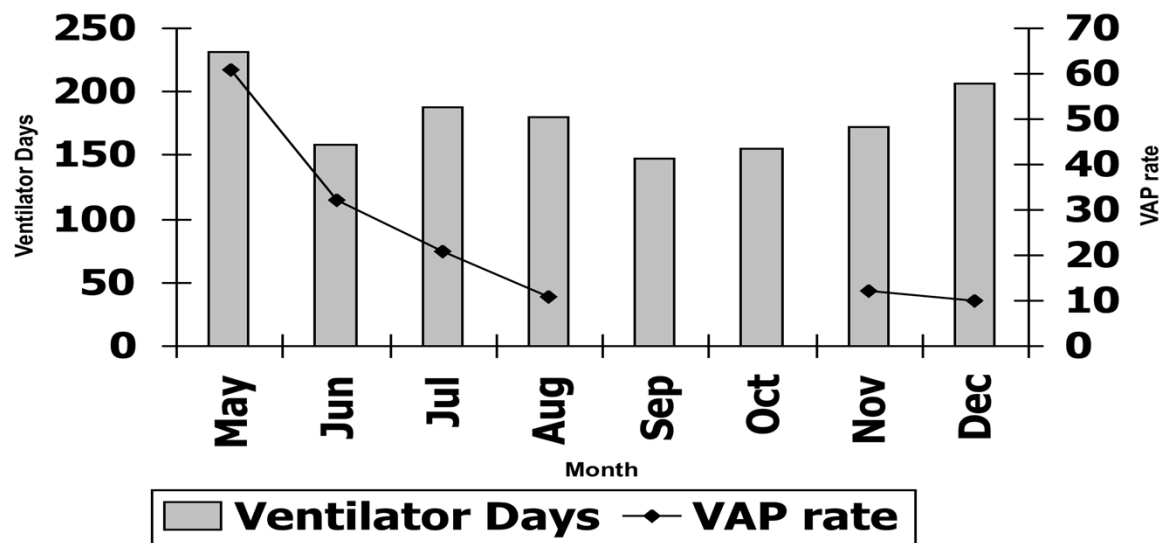


- Infection control basics
 - Handwashing, cohorting, transmission based precautions (isolation)
- Antimicrobial stewardship
 - Preventive and empiric use
- Continued study of epidemiology
- Innovative strategies and technologies

Wound Infection Prevention and Management - Prevention



- Ventilator-associated pneumonia prevention - Air Force Theater Hospital Balad



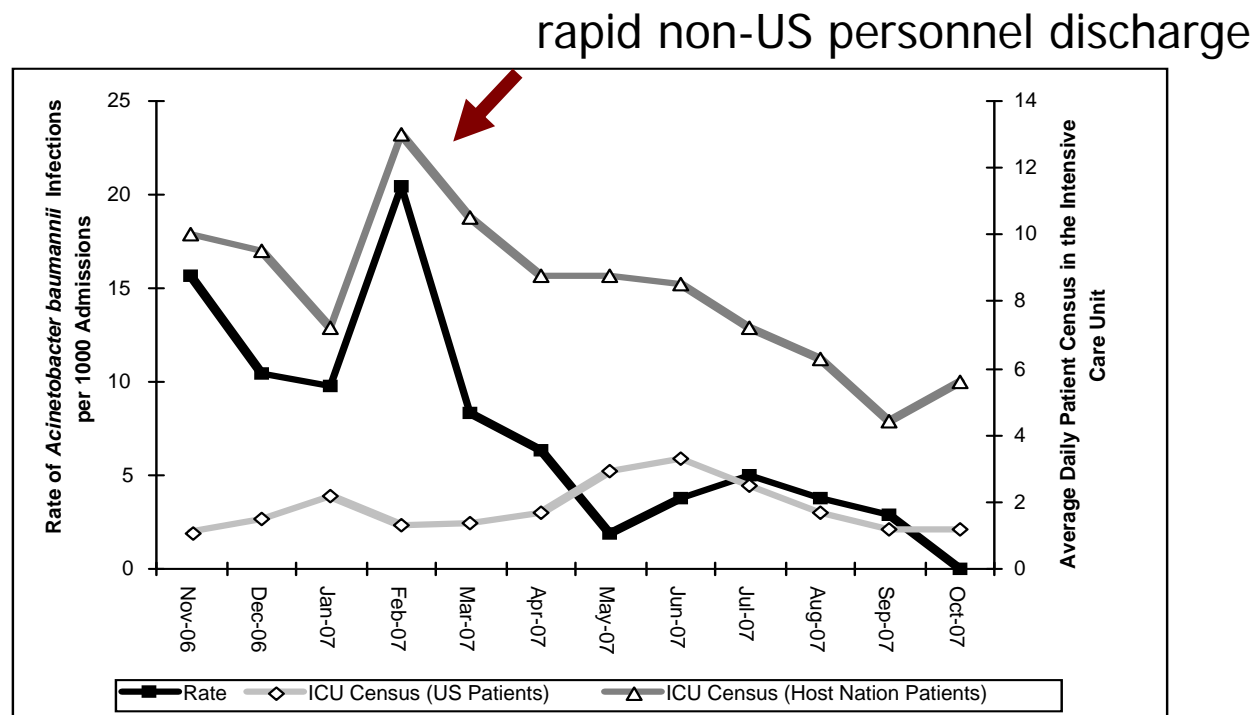
Landrum. J Trauma 2008;64:S123

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Wound Infection Prevention and Management - Prevention



- Rapid discharge of host nation patient to decrease nosocomial MDR spread



Griffith. Infect Control Hosp Epidemiol 2008;29:664

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Wound Infection Prevention and Management - Prevention



- Review of IC practice and challenges in deployed facilities (2008) (repeat missions 2009 and (planned) 2011)
 - Limited availability of trained IC personnel
 - Lack of emphasis on IC basics



Hospenthal. J Trauma 2009;66:S120

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Wound Infection Prevention and Management - Prevention



- Infection control ALARACT (2008)
 - Called for CSH Commander to assess and improve IC programs
- IC teleconsultation service established (2008)
 - infect.cntrl.consult@us.army.mil
- Web resources (infection control/treatment guidelines) (www.afids.org/links3.htm) (2008)



Wound Infection Prevention and Management - Prevention



- Infection Control in the Deployed Setting course developed (2008)
 - AMEDD C&S course 6A-F22, "Infection Control in a Deployed Environment"
 - 5-day short course for deploying Infection Control Officers (ICOs)
 - Nine classes held to date at BAMC
 - 46 USA/USAF graduates

Wound Infection Prevention and Management - Prevention



- HQDA EXORD 328-10 Infection Control Officers In Deploying Combat Support Hospitals (2010)
 - Requires CSH to have trained ICOs at each deployed location
- Deployment IC SOP adopted by USFOR-A (2010)

Wound Infection Prevention and Management



- Current epidemiology
- Prevention efforts
- Management efforts

Wound Infection Prevention and Management - **Diagnostics**



- Study of microbiology and immunological response/pathophysiology
- Predict when wounds can be safely closed
- Predict whether bacteria are contaminating, colonizing, or infecting wounds (who to treat)

Wound Infection Prevention and Management - **Diagnostics**



- Prediction of when wounds can be safely closed

TABLE V Comparison of Effluent Cytokine Concentrations Between Healed and Dehisced Wounds (N = 50)

	Concentration (Mean and Standard Deviation) (pg/mL)		P Value*
	Healed	Dehisced	
RANTES protein	1372 ± 1056	410.4 ± 350.5	<0.05
Amino-procalcitonin	18.0 ± 19.3	169.3 ± 59.8	<0.05
IL-13	12.0 ± 14.8	6.00 ± 2.78	<0.05
*Student t test.			

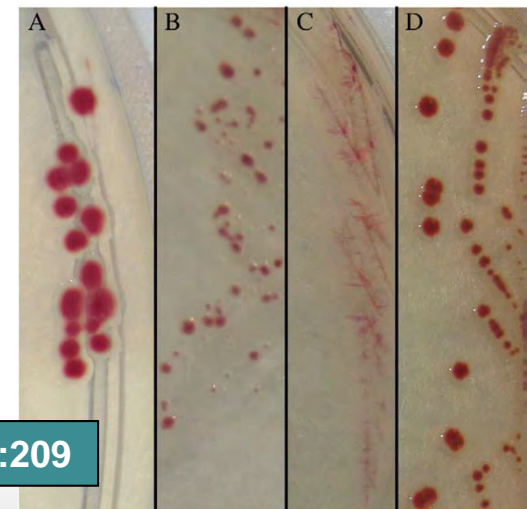
Fosberg. J Bone Joint Surg Am 2008;90:580

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Wound Infection Prevention and Management - **Diagnostics**



- Bioburden/microbiome studies
- Studies of resistance and virulence genes
- Special media (e.g., CHROMagar)
- PCR-based diagnostics



Akers. Diagn Microbiol Infect Dis 2010;67:209

Wound Infection Prevention and Management - Treatment



- Treatment of contamination or colonization (prevention)
 - Antibiotic timing and delivery (local and systemic)
 - Irrigation timing and pressure
 - Immunomodulation
 - Prevention or disruption of biofilms
- In vitro, animal models, retrospective and prospective clinical trials

Wound Infection Prevention and Management - Treatment



- NIAID-USU Infectious Disease Clinical Research Program (IDCRP)
 - Multicenter clinical trials group
 - DoD-VA Trauma Infectious Disease Outcome Study (TIDOS)
 - Preventive use of chlorhexidine clothes in military trainees



Whitman. Infect Control Hosp Epidemiol 2010;31:1207

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Wound Infection Prevention and Management - Treatment



- Orthopaedic Extremity Trauma Research Program (OETRP, formerly OTRP) (2006)
 - Reduction in wound infection
 - Multicenter clinical trials group
 - FLOW (Fluid Irrigation Techniques in Patients with Open Fracture Wounds) study
 - Local therapies to prevent infections and promote wound healing

AAOS AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
AMERICAN ASSOCIATION OF ORTHOPAEDIC SURGEONS



Wound Infection Prevention and Management - Treatment



- Major Extremity Trauma Research Consortium (METRC)
 - Supported by DoD and OETRP funding, including through PRORP
 - Prevention and treatment of acute and chronic Infections
 - Multicenter clinical trials group
 - Wound bioburden study
 - Randomized trial of oral versus IV antibiotics for wound infection with hardware in place (POvIV)



Wound Infection Prevention and Management - **Treatment**



- Peer Reviewed Orthopaedic Research Program (PRORP)
 - DoD CDMRP program
 - Non-invasive thermal ablation of osteomyelitis
 - Novel agents to inhibition of orthopaedic implant infections (e.g., host defense peptides, bacterial collagen-like proteins)
 - Novel agents to prevent biofilms

Wound Infection Prevention and Management - Treatment



- In vitro - antibiotic calcium sulfate pellets
- In vivo (animal)
 - Timing of antibiotics/debridement
 - Use of colistin beads in osteomyelitis
 - Resorbable antibiotic chitosan sponge

Jackson. J Orthop Res 2009;27:903

Brown. J Surg Orthop Adv 2010;19:18

Crane. J Orthop Res 2009;27:1008

Stinner. J Orthop Trauma 2010;24:592

Wound Infection Prevention and Management - Treatment



- Clinical, retrospective
 - Vancomycin/amikacin dosing in burn patients undergoing continuous venovenous hemofiltration (CVVH)
 - Use of external fixation in the combat setting

Wound Infection Prevention and Management - **Way Forward**



- Way forward
 - Source of MDR bacteria colonization and infection requires additional study
 - Infection control measures across the Military Health System (MHS) need to be continually improved and emphasized
 - Better understanding of the pathophysiology of wound infections is needed
 - Improved diagnostic and therapeutic modalities are needed

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DoD RDT&E Investments in Wound Infection Prevention & Management

The Quadruple Aim: Working Together, Achieving Success

COL Julia Lynch, Director Military Infectious Diseases Research Program, JPC2 Chair

24JAN2011



RDT&E for countermeasures to treat & manage wound infections



- FY08
 - Joint Force Health Protection, GDF report (Guide for Development of the Force)
 - Aim: address prevention, diagnosis, treatment, and mitigation of deployment-related injuries and psychological health concerns
 - Outlined validated gaps deemed likely addressable by increased investment in military medical R&D
 - “War Supplemental”
 - One-time appropriation of Congressional Special Interest funding

RDT&E for countermeasures to treat & manage wound infections



- **MIDRP Program Area W – ASAALT established FY10**
 - Strategic Plan: Conduct research leading to the development of measures to prevent wound infections and sepsis and nosocomial transmission of bacteria.
 - FY10 Research Objectives:
 - Determine mechanisms of biofilm formation in wounds and evaluate in-vitro methods of mitigation
 - *In-vitro* analysis of novel therapies for wound infections
 - Characterize basic pathophysiologic mechanisms of Gram negative bacteria
 - Develop methods to understand the dynamics of microbial communities in infected & healing wounds

RDT&E for countermeasures to treat & manage wound infections



- **Defense Health Program enhancement (DHPE)**
 - New, sustained program initiated in FY10
 - Based on GDF gaps
- **Objectives:**
 - To discover and explore innovative approaches to protect, support, and advance the health and welfare of military personnel, families, and communities
 - To accelerate the transition of medical technologies into deployed products
 - To accelerate the translation of advances in knowledge into new standards of care for injury prevention, treatment of casualties, rehabilitation, and training systems that can be applied in theater or in the clinical facilities of the Military Health System (MHS)

RDT&E for countermeasures to treat & manage wound infections



- **Infectious Diseases DHPe TASKS Areas:**
 - Wound Infection Prevention and Management
 - Antimicrobial Countermeasures
 - Rapid Screening of Fresh Whole Blood
 - Diagnostic Systems for Infectious Diseases
 - Acute Respiratory Disease
 - Innovative Immuno-Chemo Prophylaxis

RDT&E for countermeasures to treat & manage wound infections



■ Wound Infection Prevention & Management:

Fundamental & applied research to develop tools & practices that prevent infections and/or guide clinical wound management decisions.

■ Expected Outcomes:

- Discovery & characterization of host immune response biomarkers associated with infection to inform clinical wound-management decisions (e.g., optimal wound closure time)
- Development of tools for:
 - early detection of multidrug-resistance organisms (MDROs),
 - identification of nosocomial pathogens,
 - characterization of antimicrobial resistance patterns

RDT&E for countermeasures to treat & manage wound infections



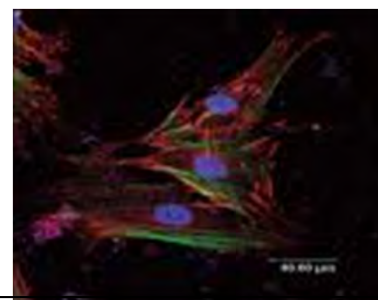
■ Wound Infection Prevention & Management:

■ Expected Outcomes:

- Development of novel environmental treatments to prevent/eliminate pathogen contamination from military medical settings.
- Development of an *in vivo* model for polytrauma/blast wound infection



Staphylococcus aureus

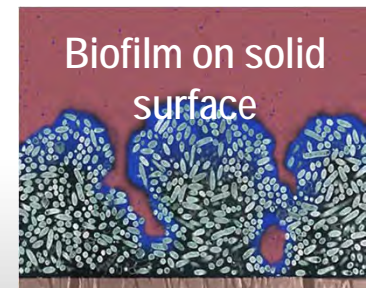


Confocal image of osteoblast cells attaching on silicon-substituted hydroxyapatite nanocrystals

RDT&E for countermeasures to treat & manage wound infections



- **Antimicrobial Countermeasures**: Fundamental & applied research to develop therapies to treat wound infections
 - *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, extended-spectrum beta-lactamase producers, & *Klebsiella pneumoniae*.
- **Expected Outcomes**
 - a) Identification & characterization of microbial virulence factors & other potential therapeutic targets of metabolic or signaling pathways associated with wound infection & biofilm processes.

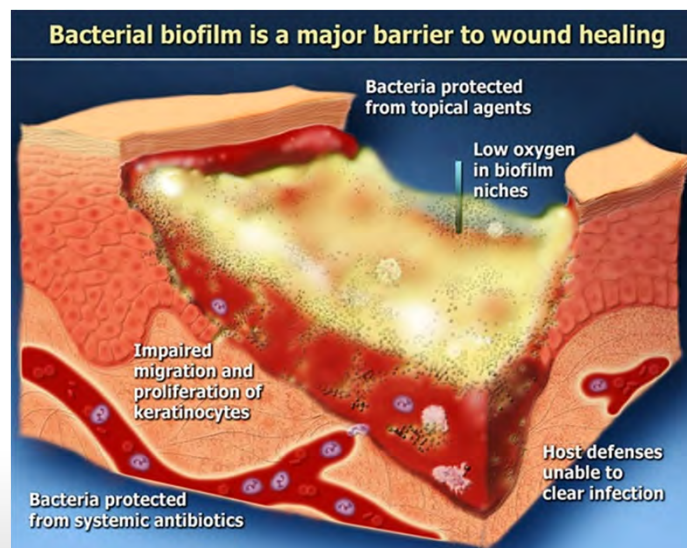


RDT&E for countermeasures to treat & manage wound infections

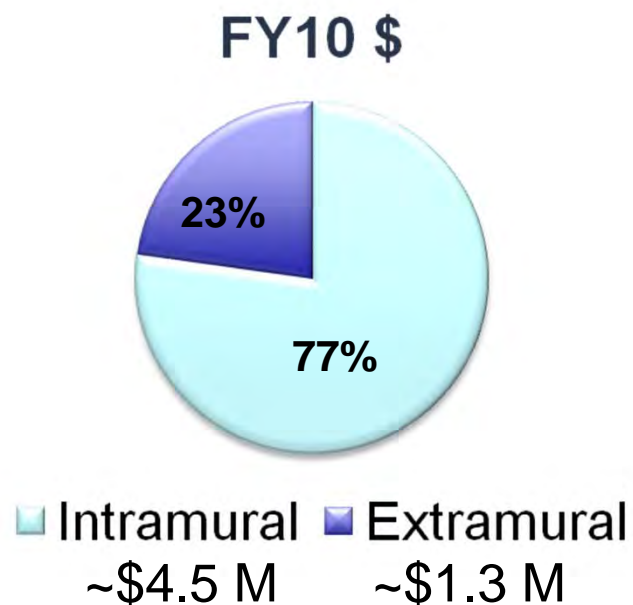


■ **Antimicrobial Countermeasures:**

- b) Identification of novel therapeutics (e.g., drugs) to mitigate wound infection & biofilm processes.
- c) Preference is for discoveries applicable to polymicrobial infections & topical treatment approaches.



FY10 DHPe Funding profile: Wound Infection Prevention and Management task area



Total \$5.8M

Intramural

WRAIR
NRL
NMRC
AFIP

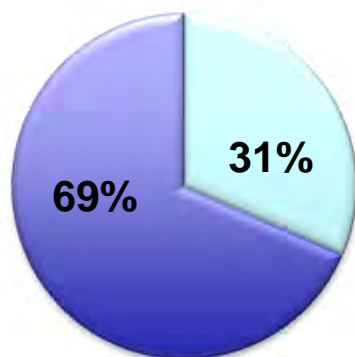
Extramural

UC Davis, School of Medicine

FY10 DHPe Funding profile: Antimicrobial Countermeasures task area



FY10 \$



■ Intramural ~\$6.5 M
 ■ Extramural ~\$14.1 M

Total \$20.6M

Intramural

WRAIR
ISR
NRL

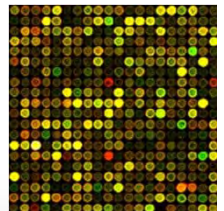
Extramural

Aridis Pharmaceuticals, LLC
North Carolina State University
University of Pennsylvania
Iasis Molecular Sciences
University of Michigan
Mote Marine Laboratory
Colorado State University
University of MD; Biotechnology Institute
Akebia Therapeutics
University of Toronto
New Mexico Institute of Mining & Technology

Key Accomplishments



- **WRAIR**: Developed a *novel osteomyelitis model* to study effects of MDR bacteria infection on osteoblast differentiation
 - Model will facilitate study of gene expression changes during bone differentiation in the context of infection, and provide a system for the study of therapeutic effects of agents.
 - May accelerate development of treatment & management options for osteomyelitis due to MDRO
- **NRL**: Antimicrobial Resistance Determinant Microarray (ARDM)
 - New technology for rapid screening of microbial or clinical samples for a broad range of antibiotic resistance genes
 - Promising as a useful tool for clinicians in selecting the best antibiotic therapy before the resistance phenotype is available



Key Accomplishments



- **WRAIR, WRAMC, JHU: Arbekacin Treatment-IND**
 - Arbekacin, approved for use in Japan, has recently been demonstrated by WRAMC to be effective against several MDR bacterial species.
 - A collaborative effort between researchers at WRAIR, WRAMC, and JHU is preparing a treatment IND for submission to FDA in 2011.
- **WRAIR: Recombinant human PON1 (quorum sensing molecule) inhibits formation and/or disruption of bacterial biofilms *in vitro***
 - PON1 (100 mg/ml) *inhibited* the formation of biofilms
 - *A. baumannii* & *P. aeruginosa*
 - Human PON1 worthy of investigating as an anti-biofilm agent for treating chronic wound infections.

Key Accomplishments



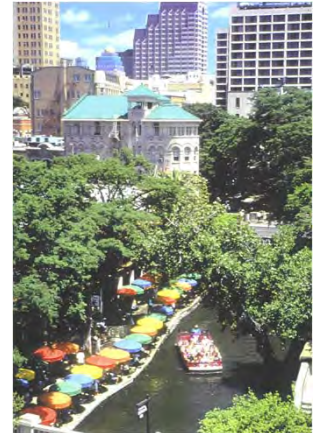
- **WRAIR:** Iron chelator (VK28; human use approved for other treatment) is effective against MDR bacteria *in vitro*
 - Works in synergy with conventional antibiotics
 - converted *Acinetobacter baumannii* once resistant to kanamycin & gentamicin to susceptibility
 - Compound in Phase I clinical testing
 - Iron chelators may prove useful in treating MDROs *in vivo*, & maybe even biofilms.
- **The Scripps Research Institute:** Synthetic derivatives of arylomycin (inhibitor of bacterial type I signal peptidase) display broad-spectrum antibiotic activity
 - Arylomycin-based drugs may reduce virulence while simultaneously killing bacteria.

RDT&E for countermeasures to treat & manage wound infections



■ DHPe-sponsored Wound Symposium

- 2-4 MAY 2011; San Antonio, TX
- Program planning coordinated with AFIDS
- Goals:
 - Assess Progress: FY10 DHPe + FY08 War Supplemental
 - Facilitate collaboration: intramural and extramural
 - Re-assess research gaps



■ Anticipate second round of DHPe funding in FY12

RDT&E for countermeasures to treat & manage wound infections



- Thank you for your attention....

Military Infectious Diseases (JTTCG-2)

Joint Program Committee



Joint Program Committee (JPC2) :

- Army Representative on JTTCG-2 (Chair of the committee and Director RAD-1)
- Navy representative on JTTCG-2
- Air Force representative on JTTCG-2
- ID consultant to USA SG
- ID consultant to USAF SG
- ID consultant to USN SG
- MIDRP Program W Research Coordinator
- USAMMDA
- AMEDD C&S
- AFHSC
- NIH
- OSD[HA]
- ODATSD (CBD/CD)
- VA
- IDCPR (NIAID/USUHS)